REMARKS

Claims 1-74 were originally filed and were subject to restriction. In response to the Restriction Requirement dated 9 July 2001, Applicants elected with traverse the claims of Group I, claims 1-21, 30, and 42-74. Applicants note with appreciation that the Examiner found claims 4, 8, 16-20, and 53 allowable as rewritten in independent form. To facilitate prosecution of this allowable subject matter, claims 1, 22-29, 31-41, 52, and 63 are canceled above, without prejudice or disclaimer. Claims 2, 3, 5-14, 16-21, 30, 42-51, 53-62, and 64-74 are amended above. New claim 75 is added. Thus, claims 2-21, 30, 42-51, 53-62, and 64-75 are now pending.

Justification for the amendments is as follows. The amendments to the specification in the paragraphs beginning at pages 40 and 61 were made to properly reference co-pending U.S. Patent Application Serial Nos. 09/709,700 and 09/710,249, respectively. The remaining amendments to the specification were made to correct grammatical and typographical errors.

Claims 1, 22-29, 31-41, 52, and 63 are canceled above without prejudice to their renewal. Applicants reserve the right to pursue the subject matter of these claims in continuing applications. Claims 7, 8, 12, and 16-20 are amended above to no longer depend from canceled claim 1. Claim 20 is further amended to include the limitations of canceled claim 1, as suggested by the Examiner. Claims 2, 3, 5, 6, 9-11, 13, 14, 42-51, 54-62, 64-68, and 70-74 are amended above to depend from claim 20, which the Examiner has indicated is allowable as amended. Claim 69 is amended above to depend from amended claim 7. Claim 53 is amended above to include the limitations of canceled claim 52, as suggested by the Examiner.

Support for the term "recombinant human gelatin" as recited in amended claims 2, 3, 5, 6, 9-11, 13, 14, 42-51, 54-62, 64-68, and 70-74 is found throughout the specification, for example, at page 7, lines 38-39; at page 22, lines 26-29; at page 22, lines 36-37; at page 28, lines 22-24; and in claims 20 and 53 as originally filed. Claim 12 is amended to correct the spelling of the word "homogeneous" as directed by the Examiner. Claim 7 is amended to specify that "proline" amino acid residues are hydroxylated. Support for this amendment can be found throughout the specification, for example, at page 25, lines 20-22. Support for claim 10 as amended above can

be found throughout the specification, for example, at page 38, lines 13-17, and in Examples 9, 10, and 11.

Claim 14 is amended to recite the term "is obtained from" as suggested by the Examiner. Claims 21 and 30 are amended to delete reference to non-elected sequences as required by the Examiner. Claim 70 is amended to no longer recite the term "fully-hydroxylated." Support for claim 8 as amended can be found throughout the specification, for example, at page 25, line 37 to page 26, line 8; at page 26, lines 16-18; and at page 80, lines 31-33. Support for the stabilizer of new claim 75 can be found in the specification, for example, at page 58, lines 14-15, and at page 61, lines 24-27.

All other amendments to the claims were made to correct mere grammatical and typographical errors or for consistency of claim language. No new matter is added by any of the above amendments.

I. Objection to claims 4, 8, 16-20, and 53

The Examiner stated that "[c]laims 4, 8, 16-20 and 53...would be allowable if rewritten in independent form including all of the limitations of the [rejected] base claim...." (Office Action, page 8.) The Examiner's indication that these claims are allowable as amended is appreciated. Applicants note that claim 4 is an independent claim as originally filed, and assume the Examiner intended to state that this claim is allowable as written. Claims 8, 16-20, and 53 are amended above as suggested by the Examiner. Therefore, the objection to claims 4, 8, 16-20, and 53 is overcome, and Applicants respectfully request withdrawal of the objection to these claims.

II. Oath/Declaration

The Examiner stated "[a] new oath or declaration in compliance with 37 CFR 1.67(a)...is required" because "non-dated alterations have been made to the address of Invertor [sic], James W. Polarek." (Office Action, page 2.) Accordingly, attached herewith is an executed declaration under 37 CFR 1.67(a).

III. Objection to claim 12

The Examiner objected to claim 12 "because the term 'homogeneous' is misspelled." (Office Action, page 3.) Accordingly, claim 12 is amended above to recite "homogeneous." The objection to claim 12 is thus overcome, and withdrawal of the objection is respectfully requested.

IV. Rejection of claims 7, 10, 11, 14, 21, 30, 63, 69, and 70 under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 7, 10, 11, 14, 21, 30, 63, 69, and 70 under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants address the rejection of each of the claims in turn.

The Examiner rejected claims 7 and 69 as being indefinite for reciting the term "partially hydroxylated." In particular, the Examiner stated "it is unclear to what extent the recombinant gelatin is hydroxylated as to 'partially hydroxylated' and which amino acid residues are hydroxylated." (Office Action, page 3.) Applicants submit that the term "partially hydroxylated" as recited in claim 7 would be understood by a person of skill in the art in view of the specification. The specification states "[t]he present invention comprises fully-hydroxylated, partially-hydroxylated, and non-hydroxylated recombinant gelatins" and discloses "recombinant gelatins ranging from non-hydroxylated to fully-hydroxylated." (See the specification at page 34, lines 21-22, and at page 26, lines 17-18.) One of skill in the art would understand, in view of the specification, and as known by one of skill in the art, that the term "partially hydroxylated" means a level of hydroxylation between non-hydroxylated and fully-hydroxylated. Therefore, the term "partially hydroxylated" is clear and definite. In addition, claim 7 and claim 69, which as amended depends directly from claim 7, are amended above to specify that the "proline" amino acid residues are hydroxylated. In view of the above, claims 7 and 69 are thus clear and definite. As claims 7 and 69 are clear and definite, the rejection to these claims under 35 U.S.C. §112 is overcome, and Applicants respectfully request withdrawal of this rejection.

The Examiner rejected claim 10 as being indefinite for reciting the term "fully hydrolyzed." The term "fully hydrolyzed" does not appear in amended claim 10 above. The rejection of claim 10 under 35 U.S.C. §112 is thus moot.

The Examiner rejected claim 11 as being indefinite for reciting the phrase "partially hydrolyzed." The Examiner stated "it is unclear to what extent the recombinant gelatin is hydrolyzed as to 'partially hydrolyzed.'" (Office Action, page 4.) "Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification." (See, MPEP 2173.05(b), page 2100-196, 8th edition, August 2001.) The term "partially hydrolyzed" is widely used and understood in the art. For example, U.S. Patent No. 4,147,772, cited by the Examiner in the present Office Action, refers to "partially hydrolyzed gelatin." (See, e.g., column 1, lines 65-66; column 2, lines 14-16; column 2, lines 46-50; and claims 1, 5, and 6.) Applicants submit that the term "partially hydrolyzed" is thus a term that would be well understood by a person of skill in the relevant art when read in light of the specification. Therefore, claim 11 is clear and definite and Applicants respectfully request withdrawal of the rejection to claim 11 under 35 U.S.C. §112.

The Examiner rejected claim 14 as being indefinite for use of the term "is derived from," and suggested the claim be amended to recite "is obtained from." (Office Action, page 4.) Accordingly, the phrase "is derived from" is replaced above with the phrase "is obtained from" as suggested by the Examiner. Therefore, withdrawal of the rejection to claim 14 under 35 U.S.C. §112 is respectfully requested.

The Examiner rejected claims 21 and 30 as being indefinite "because the claim[s] contain[s] non-elected sequences." (Office Action, page 4.) Claims 21 and 30 are amended above to recite elected sequences SEQ ID NOs:18 and 29, respectively. The rejection of claims 21 and 30 is thus overcome, and Applicants respectfully request withdrawal of the rejection to these claims under 35 U.S.C. §112.

The Examiner rejected claim 63 as being indefinite for reciting the terms "device" and "a subject." Claim 63 is canceled above, and this rejection is therefore moot.

The Examiner rejected claim 70 as being indefinite for reciting "fully-hydroxylated." The term "fully-hydroxylated" no longer appears in amended claim 70. The rejection of claim 70 is thus rendered moot.

In summary, all of the rejections under 35 U.S.C. §112 having been rendered moot or overcome by the above amendments and arguments, withdrawal of the rejection of claims 7, 10, 11, 14, 21, 30, 63, 69, and 70 under 35 U.S.C. §112, second paragraph, is respectfully requested.

V. Rejection of claims 1, 44, 64, 65, 67, and 68 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 44, 64, 65, 67, and 68 under 35 U.S.C. §102(b) as being anticipated by Piliero *et al.*, U.S. Patent No. 5,330,773 (the '773 patent). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 44, 64, 65, 67, and 68 are amended above to depend from claim 20. The '773 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '773 patent does not anticipate claim 20, or claims 44, 64, 65, 67, and 68, which depend directly from claim 20. As the '773 patent does not anticipate claims 44, 64, 65, 67, and 68, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

VI. Rejection of claims 1, 64, and 66 under 35 U.S.C. §102(b)

The rejection of claims 1, 64, and 66 under 35 U.S.C. §102(b) as being anticipated by Grossman *et al.*, U.S. Patent No. 5,194,282 (the '282 patent), is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 64 and 66 are amended above to depend from claim 20. The '282 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '282 patent does not anticipate claim 20. Claims 64 and 66,

which depend directly from claim 20, are also not anticipated by this reference. As the '282 patent does not anticipate claims 64 and 66, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

VII. Rejection of claims 1, 43, 54, 55, and 68 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 43, 54, 55, and 68 under 35 U.S.C. §102(b) as being anticipated by Russell *et al.*, U.S. Patent No. 5,827,852 (the '852 patent). This rejection of is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 43, 54, 55, and 68 are amended above to depend from claim 20. The '852 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '852 patent does not anticipate claim 20, or claims 43, 54, 55, and 68, which depend directly from claim 20. As the '852 patent does not anticipate claims 43, 54, 55, and 68, and as claim 1 is canceled above, Applicants respectfully request withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b).

VIII. Rejection of claims 1, 42, 45, 64, and 68 under 35 U.S.C. §102(b)

The rejection of claims 1, 42, 45, 64, and 68 under 35 U.S.C. §102(b) as being anticipated by Mason *et al.*, U.S. Patent No. 5,565,227 (the '227 patent), is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 42, 45, 64, and 68 are amended above to depend from claim 20. The '227 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '227 patent does not anticipate claim 20, or claims 42, 45, 64, and 68, which depend directly from claim 20. As the '227 patent does not anticipate claims 42, 45, 64, and 68, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

IX. Rejection of claims 1, 5, 6, 45, 46, 49, 64, and 68 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 5, 6, 45, 46, 49, 64, and 68 under 35 U.S.C. §102(b) as being anticipated by Todd, U.S. Patent No. 4,356,202 (the '202 patent). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 5, 6, 45, 46, 49, 64, and 68 are amended above to depend from claim 20. The '202 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '202 patent does not anticipate claim 20, and further does not anticipate claims 5, 6, 45, 46, 49, 64, and 68, which depend directly from claim 20. As the claims 5, 6, 45, 46, 49, 64, and 68 are not anticipated by the '202 patent, and as claim 1 is canceled above, Applicants respectfully request withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b).

X. Rejection of claims 1 and 51 under 35 U.S.C. §102(b)

The rejection of claims 1 and 51 under 35 U.S.C. §102(b) as being anticipated by Bolinger, U.S. Patent No. 3,578,492 (the '492 patent), is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claim 51 is amended above to depend from claim 20. The '492 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '492 patent does not anticipate claim 20, or claim 51, which depends directly from claim 20. As the '492 patent does not anticipate claim 51, and as claim 1 is canceled above, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(b).

XI. Rejection of claims 1, 47, 48, 49, and 71 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 47, 48, 49, and 71 under 35 U.S.C. §102(b) as being anticipated by Zviak *et al.*, U.S. Patent No. 3,840,338 (the '338 patent). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 47, 48, 49, and 71 are amended above to depend from claim 20. The '338 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '338 patent does not anticipate claim 20, or claims 47, 48, 49, and 71, which depend directly from claim 20. As the '338 patent does not anticipate claims 47, 48, 49, and 71, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

XII. Rejection of claims 1, 45, 50, and 72 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 45, 50, and 72 under 35 U.S.C. §102(b) as being anticipated by Helmstetter, U.S. Patent No. 4,055,554 (the '554 patent). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 45, 50, and 72 are amended above to depend from claim 20. The '554 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '554 patent does not anticipate claim 20, or claims 45, 50, and 72, which depend directly from claim 20. As the '554 patent does not anticipate claims 45, 50, and 72, and as claim 1 is canceled above, Applicants respectfully request withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b).

XIII. Rejection of claims 1 and 73 under 35 U.S.C. §102(b)

The rejection of claims 1 and 73 under 35 U.S.C. §102(b) as being anticipated by McAleer *et al.*, U.S. Patent No. 4,147,772 (the '772 patent), is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claim 73 is amended above to depend from claim 20. The '772 patent does not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, the '772 patent does not anticipate claim 20, or claim 73, which

depends directly from claim 20. As the '772 patent does not anticipate claim 73, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

XIV. Rejection of claims 1, 52, 57, and 74 under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 52, 57, and 74 under 35 U.S.C. §102(b) as being anticipated by Beyer *et al.* (Br. J. Anesthesia 78:44-50 (1997)). This rejection is respectfully traversed.

Claims 1 and 52 are canceled above and the rejection is therefore moot as to these claims. Claims 57 and 74 are amended above to depend from claim 20. Beyer *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Beyer *et al.* do not anticipate claim 20, or claims 57 and 74, which depend directly from claim 20. As Beyer *et al.* do not anticipate claims 57 and 74, and as claims 1 and 52 are canceled above, Applicants respectfully request withdrawal of the rejection to these claims as being anticipated by this reference under 35 U.S.C. §102(b).

XV. Rejection of claims 1, 52, 61, and 62 under 35 U.S.C. §102(b)

The rejection of claims 1, 52, 61, and 62 under 35 U.S.C. §102(b) as being anticipated by Di Silvio *et al.* (J. Mater. Sci.: Mater. Med. 5:819-823 (1994)), is respectfully traversed.

Claims 1 and 52 are canceled above and the rejection is therefore moot as to these claims. Claims 61 and 62 are amended above to depend from claim 20. Di Silvio *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Di Silvio *et al.* do not anticipate claim 20, or claims 61 and 62, which depend directly from claim 20. As Di Silvio *et al.* do not anticipate claims 61 and 62, and as claims 1 and 52 are canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

XVI. Rejection of claims 1 and 56 under 35 U.S.C. §102(b)

The Examiner rejected claims 1 and 56 under 35 U.S.C. §102(b) as being anticipated by Kanatani *et al.* (Agri. Biol. Chem. 53:1185-1187 (1989)). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claim 56 is amended above to depend from claim 20. Kanatani *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Kanatani *et al.* do not anticipate claim 20, or claim 56, which depends directly from claim 20. As Kanatani *et al.* do not anticipate claim 56, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(b) is respectfully requested.

XVII. Rejection of claims 1-3, 9, 11, and 13-15 under 35 U.S.C. §102(a)

The rejection of claims 1-3, 9, 11, and 13-15 under 35 U.S.C. §102(a) as being anticipated by Werten *et al.* (Yeast 15:1087-1096 (August, 1999)), is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claim 15 and amended claims 2, 3, 9, 11, 13, and 14 depend from claim 20. Werten *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Werten *et al.* do not anticipate claim 20, claims 2, 3, 9, 11, and 13-15, which depend from claim 20. As Werten *et al.* do not anticipate claims 2, 3, 9, 11, 13-15, and as claim 1 is canceled above, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(a) by this reference.

XVIII. Rejection of claims 1, 59, and 60 under 35 U.S.C. §102(a)

The Examiner rejected claims 1, 59, and 60 under 35 U.S.C. §102(a) as being anticipated by Luks *et al.* (Am. J. Obstet. Gynecol. 181:995-996 (October 1999)). This rejection is respectfully traversed.

Claim 1 is canceled above and the rejection is therefore moot as to this claim. Claims 59 and 60 are amended above to depend from claim 20. Luks *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Luks *et al.* do not anticipate claim 20, or claims 59 and 60, which depend directly from claim 20. As Luks *et al.* do not anticipate claims 59 and 60, and as claim 1 is canceled above, withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(a) is respectfully requested.

XIX. Rejection of claims 1, 52, and 58 under 35 U.S.C. §102(a)

The rejection of claims 1, 52, and 58 under 35 U.S.C. §102(a) as being anticipated by Mligilche *et al.* (East African Med. J. 76:400-406 (July, 1999)), is respectfully traversed.

Claims 1 and 52 are canceled above and the rejection is therefore moot as to these claims. Claim 58 is amended above to depend from claim 20. Mligilche *et al.* do not disclose "recombinant human gelatin" as recited in claim 20, which the Examiner has indicated to be allowable as amended above. Therefore, Mligilche *et al.* do not anticipate claim 20, or claim 58, which depends directly from claim 20. As Mligilche *et al.* do not anticipate claim 58, and as claims 1 and 52 are canceled above, Applicants respectfully request withdrawal of the rejection of these claims as being anticipated by this reference under 35 U.S.C. §102(a).

CONCLUSION

In view of the foregoing, Applicants submit that the claims are fully in condition for allowance and request early notification to that effect. The Examiner's indication that claims 4, 8, 16-20, and 53 are allowable is much appreciated. If the Examiner has any questions regarding the present communication or the above-referenced application, please call Applicants' Attorney directly at 650-866-7254.

Respectfully submitted,

DATE: 16 August 02

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

At page 4, the paragraph beginning at line 13.

A more homogeneous product, and one produced by more reproducible means, would be desirable. The availability of a homogeneous [homogenous] material with reproducible physical characteristics would be desirable, for example, in various products and processes, where the availability of gelatin with specific characteristics, such as a fixed range of molecular weight, would allow for a reproducible and controlled performance. There is thus a need for a reliable and reproducible means of gelatin production that provides a homogeneous [homogenous] product with controlled characteristics.

At page 6, the paragraph beginning at line 17.

In one aspect, the present invention provides a composition comprising recombinant gelatin, wherein the recombinant gelatin comprises a homogeneous [homogenous] mixture of recombinant gelatin polypeptides. In another aspect, the recombinant gelatin comprises a heterogeneous mixture of recombinant gelatin polypeptides.

At page 30, the paragraph beginning at line 37.

The present invention provides methods for designing recombinant gelatins with the physical properties desired for particular applications. In one embodiment, the present invention provides recombinant gelatins comprising uniform molecules of a specified molecular weight or range of molecular weights, and methods for producing these recombinant gelatins. Such homogeneous [homogenous] and uniform materials are advantageous in that they provide a reliable source of product with predictable performance, minimizing variability in product performance and in manufacturing parameters. Currently, gelatin from different lots must sometimes be blended in order to produce a mixture with the desired physical characteristics, such as the viscosity or gel strength, etc., provided by a particular molecular weight or molecular weight range.

At page 38, the paragraph beginning at line 13.

In various aspects, the present invention provides recombinant gelatin that is non-hydrolyzed, fully hydrolyzed, or hydrolyzed to varying degrees, such as gelatins that are a mixture of hydrolyzed and non-hydrolyzed products. Additionally, the present invention provides methods of producing recombinant gelatins with varying degrees of hydrolysis. (See Examples 9 and 10.) Gelatin hydrosylates are typically cold water-soluble and are used in a variety of applications, particularly in the pharmaceutical and food industries, in which a gelatin with non-gelling properties is desirable. Gelatin hydrolysates are used in the pharmaceutical industry in film-forming agents, microencapsulation [micro-encapsulation] processes, arthritis and joint relief formulas, tabletting, and various nutritional formulas. In the cosmetics industry, gelatin hydrolysates are used in shampoos and conditioners, lotions and other formulations, including lipsticks, and in fingernail formulas, etc. Gelatin hydrolysates appear as nutritional supplements in protein and energy drinks and foods; are used as fining agents in wine, beer, and juice clarification; and are used in the microencapsulation [micro-encapsulation] of additives such as food flavorings and colors. Gelatin hydrosylates are used in industrial applications for their film-forming characteristics, such as in coatings of elements in semiconductor manufacture, etc.

At page 39, the paragraph beginning at line 18.

In one aspect of the present invention, it is desirable to create a homogeneous [homogenous] gelatin composed of fragments synthesized from collagen constructs lacking platelet activation regions. Such gelatin could be included, for example, in products associated with anastomosis and vascular grafting, etc., including coatings for stents and graft devices. Such products can be associated with deleterious side effects, for example, thrombosis, that can develop in association with the use of such products as a result of the platelet-aggregating regions present in the collagenous product. In one aspect, the present invention provides for a method of producing a recombinant gelatin which can provide support for cell attachment when used in a stent or similar device, but which does not include platelet-reactive regions, thus minimizing the risk of platelet

aggregation. (See Example 2.) Therefore, the present invention provides in one embodiment for a stent coating comprising recombinant gelatin. In a preferred embodiment, the recombinant gelatin is recombinant human gelatin. In some instances, such as various wound care applications, it could be desirable to provide recombinant gelatin comprising domains capable of inducing specific aggregating activities.

At page 39, the paragraph beginning at line 33.

A gelatin of the present invention could be expressed from collagen constructs that did not encode the regions recognized by the $\alpha 2\beta 1$ receptor, or from constructs with one or with multiple copies of such regions, thus providing a homogeneous [homogenous] and consistent gelatin product without or with reduced platelet aggregation and activation. In one aspect, the present invention provides for the production of recombinant gelatin, either through direct expression of gelatin or through processing of gelatin from collagenous polypeptides, through the use of highly efficient recombinant expression. The present production methods, as opposed to current methods of extraction, offer extreme flexibility, as any one of a number of expression systems can be used. The production material is accessible, for example, in yeast or plant biomass. Secretion in certain production systems can be optimized, for example, by dictating the uniform size of particular gelatin molecules to be produced according to the present methods. In various embodiments, the present gelatins or the polypeptides from which these gelatins are derived, are produced in expression systems including, but not limited to, prokaryotic expression systems, such as bacterial expression systems, and eukaryotic expression systems, including yeast, animal, plant, and insect expression systems. Expression systems such as transgenic animals and transgenic plants are contemplated.

At page 40, the paragraph beginning at line 15.

The present invention provides for expression of at least one polynucleotide encoding a gelatin or a polypeptide from which gelatin can be derived in a cell. In one embodiment, the present invention provides for the expression of more than one polynucleotide encoding a gelatin or a polypeptide from which gelatin can be derived in a cell, such that recombinant gelatin containing homogeneous [that is a homogenous] or heterogeneous

polypeptides is produced. The present invention further provides for expression of a polynucleotide encoding a collagen processing or post-translational enzyme or subunit thereof in a cell. Different post-translational modifications, and different post-translational enzymes, e.g., prolyl hydroxylase, lysyl hydroxylase, etc., can effect, for example, Bloom strength and other physical characteristics of the present gelatins.

At page 40, the paragraph beginning at line 34.

Nucleic acid sequences encoding collagens have been generally described in the art. (See, e.g., Fuller and Boedtker (1981) Biochemistry 20:996-1006; Sandell et al. (1984) J Biol Chem 259:7826-34; Kohno et al. (1984) J Biol Chem 259:13668-13673; French et al. (1985) Gene 39:311-312; Metsaranta et al. (1991) J Biol Chem 266:16862-16869; Metsaranta et al. (1991) Biochim Biophys Acta 1089:241-243; Wood et al. (1987) Gene 61:225-230; Glumoff et al. (1994) Biochim Biophys Acta 1217:41-48; Shirai et al. (1998) Matrix Biology 17:85-88; Tromp et al. (1988) Biochem J 253:919-912; Kuivaniemi et al. (1988) Biochem J 252:633-640; and Ala-Kokko et al. (1989) Biochem J 260:509-516.) See also co-pending, commonly-owned application U.S. Patent Application Serial No. 09/709,700 [U.S. Application Serial No. _____], entitled "Animal Collagens and Gelatins," filed 10 November 2000, incorporated herein by reference in its entirety.)

At page 58, the paragraph beginning at line 19.

Gelatin in various edible forms has long been used in the food and beverage industries. Gelatin is used widely in various confectionery and dessert products, particularly in puddings, frostings, cream fillings, and dairy and frozen products. Gelatin serves as an emulsifier and thickener in various whipped toppings, as well as in soups and sauces. Gelatin is used as a flocculating agent in clarifying and fining various beverages, including wines and fruit juices. Gelatin is used in various low and reduced fat products, such as mayonnaise and salad dressings, as a thickener and stabilizer, and appears elsewhere as a fat substitute. Gelatin is also widely used in microencapsulation [micro-encapsulation] of flavorings, colors, and vitamins. Gelatin can also be used as a protein supplement in various high energy and nutritional beverages and foods, such as those prevalent in the weight-loss and athletic industries. As a film-former, gelatin is used in

coating fruits, meats, deli items, and in various confectionery products, including candies and gum, etc.

At page 58, the paragraph beginning at line 32.

In the cosmetics industry, gelatin appears in a variety of hair care and skin care products. Gelatin is used as a thickener and bodying agent in a number of shampoos, mousses, creams, lotions, face masks, lipsticks, manicuring solutions and products, and other cosmetic devices and applications. Gelatin is also used in the cosmetics industry in microencapsulation [micro-encapsulation] and packaging of various products.

At page 59, the paragraph beginning at line 25.

Gelatin has also been a valuable substance for use in various laboratory applications. For example, gelatin can be used in various cell culture applications, providing a suitable surface for cell attachment and growth, e.g., as a coating for plates, flasks, microbeads [micro-beads], or other substrates, or providing a suitable protein source in growth media. Hydrolyzed or low gel strength gelatin is used as a biological buffer in various processes, for example, in coating and blocking solutions used in assays such as enzyme-linked immunosorbent assays (ELISAs) and other immunoassays. Gelatin is also a component in various gels used for biochemical and electrophoretic analysis, including enzymography gels.

At page 60, the paragraph beginning at line 18.

In addition to providing a gelatin material without the immunogenecity and infectivity issues associated with animal-derived materials, the present invention allows for a reproducible source of consistent product. Specifically, the present gelatins can be presented as a homogeneous [homogenous] mixture of identical molecules. The physical characteristics desired in a particular medical application can be specifically introduced and achieved consistently. The present invention is thus able to provide a reliable and consistent product will minimize variability associated with the availability and use of current gelatin products.

At page 61, the paragraph beginning at line 24.

The recombinant gelatin of the present invention can also be used as a stabilizer in various pharmaceutical products, for example, in drugs or vaccines. (See, e.g., co-pending, commonly-owned U.S. Patent Application Serial No. 09/710,249 [U.S. Application Serial No. _____], entitled "Recombinant Gelatins in Vaccines," filed 10 November 2000, incorporated herein by reference in its entirety.) Therefore, in one embodiment, the present invention provides a stabilizing agent comprising recombinant gelatin, wherein the stabilizer is suitable for use in pharmaceutical applications. In a preferred embodiment, the recombinant gelatin is recombinant human gelatin.

At page 69, the paragraph beginning at line 13.

Gelatin is also used in microencapsulation [micro-encapsulation] of various flavors, colors, and other additives, and of vitamins.

At page 69, the paragraph beginning at line 16.

Specifically contemplated are various recombinant gelatins that can be used as stabilizing agents, thickening agents, film-forming agents, binding agents, edible coatings, gelling agents, protein supplements, emulsifying agents, microencapsulants [micro-encapsulants] for colors, flavors, and vitamins, etc., and can be used in various food supplements, including nutritional and diet supplements, and fat substitutes. In one embodiment, the gelatin of the present invention is used in the processing or packaging of, or as a component in, foods prepared for consumers with Kosher, Halal, vegetarian, or other diets that restrict the ingestion of food containing specific animal-source products.

At page 71, the paragraph beginning at line 11.

The distinctive properties of gelatin, including its ability to serve as a protective colloid, and to alter its electrical charge with changes in pH, combine to make gelatin a material suitable for use in microencapsulation [micro-encapsulation]. Gelatin and its derivatives can thus be used in a variety of microencapsulation [micro-encapsulation] devices and techniques, for example, in the microencapsulation [micro-encapsulation] of inks for carbon-free paper; fragrances for advertising and sample manufacture; chemicals used in

multi-component adhesives; and vitamins and nutritional supplements. The microencapsulation [micro-encapsulation] capabilities of gelatin and its derivatives are also useful in the manufacture of packaging materials, including packaging allowing minimal permeability for oxygen, aromas, and water vapor. Gelatin is thus widely used in flexible packaging, such as packaging for food, pharmaceuticals, and other sensitive products.

At page 72, the paragraph beginning at line 34.

Recombinant gelatins consisting of biologically active regions of collagen type III, for example, can be prepared as microfibers [micro-fibers] that consist of a uniformity, purity, and reproducibility unattainable with current collagen and gelatin sources. Microfibers derived from the present recombinant gelatins can be presented on substrates, e.g., arrays or chips, used to screen for compounds that prevent platelet aggregation through interaction with, e.g., type III collagen, or any other fibril-forming collagen. Chemical compounds, small molecules, peptides, or other biological molecules (such as antibodies) can be screened for their ability to prevent, reduce, or slow the process of clot formation or platelet aggregation, mediated by platelet interactions with specific regions within a collagen fiber, such as, for example, RGD sequences. Additionally, microarrays would also be useful for examination of the interaction of different types of integrins with various regions of collagens and gelatin microfibers [micro-fibers]. Microfibers produced from recombinant gelatins from any of the fibril-forming collagens, e.g., collagen type I, type II, type III, type V, or type XI, could be used in screening for collagen-induced platelet aggregation antagonists.

At page 74, the paragraph beginning at line 28.

The distinctive properties of gelatin, including its ability to serve as a protective colloid, and to alter its electrical charge with changes in pH, combine to make gelatin a material suitable for use in microencapsulation [micro-encapsulation]. Gelatin and its derivatives can thus be used in a variety of microencapsulation [micro-encapsulation] devices and techniques, for example, in the microencapsulation [micro-encapsulation] of fragrances for advertising and sample manufacture.

At page 87, the paragraph beginning at line 14.

As a further refinement of the heat hydrolyzed recombinant human gelatins discussed, we have demonstrated the utility of a yeast multi-gene recombinant expression methodology for the production of human gelatins with discrete fragments of the α1(I) [α1 (I)] chain of human type I collagen. This technology allowed us to produce well-defined, highly homogeneous [homogenous] gelatin fragments ranging in size from 6-65 kDa. This presents unsurpassed flexibility in terms of the size and biophysical properties of the gelatin that can be used for specific applications.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

2. (Amended) The [A] recombinant human gelatin of claim 20, wherein the recombinant human gelatin has [having] a molecular weight selected from the group consisting of about 5 kDa, about 8 kDa, about 9 kDa, about 14 kDa, about 16 kDa, about 22 kDa, about 23 kDa, about 36 kDa, about 44 kDa, and about 65 kDa.

3. (Amended) The [A] recombinant human gelatin of claim 20, wherein the recombinant human gelatin has [having] a molecular weight range selected from the group consisting of about 0 to 50 kDa, about 10 to 30 kDa, about 30 to 50 kDa, about 10 to 70 kDa, about 50 [kDa] to 70 kDa, about 50 to 100 kDa, about 100 to 150 kDa, about 150 to 200 kDa, about 200 to 250 kDa, about 250 to 300 kDa, and about 300 to 350 kDa.

4. (Reiterated) A recombinant gelatin having a molecular weight greater than 300 kDa.

5. (Amended) The [A] recombinant human gelatin of claim 20, wherein the recombinant human gelatin has [having] a Bloom strength selected from the group consisting of 50, 100, 150, 200, 250, and 300.

6. (Amended) The [A] recombinant human gelatin of claim 20, wherein the recombinant human gelatin has [having] a Bloom strength of between 0 and 100.

7. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin is partially[-] hydroxylated, and further wherein the hydroxylation is on proline residues.

8. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin has a percentage hydroxylation selected from the group consisting of 20 to 80%, 30 to 80%, 40 to 80%, 60 to 80%, 80 to 100%, 20 to 60%, 30 to 60%, 40 to 60%, 20 to 30%, 20 to 40%, and 30 to 40%.

9. (Amended) The composition of claim 20 [1], wherein the recombinant human gelatin is non-hydroxylated.

10. (Amended) The composition of claim 20 [1], wherein the recombinant human gelatin is [fully] hydrolyzed.

11. (Amended) The composition of claim 20 [1], wherein the recombinant human gelatin is partially hydrolyzed.

12. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin comprises a homogeneous [homogenous] mixture of recombinant gelatin polypeptides.

13. (Amended) The composition of claim 20 [1], wherein the recombinant human gelatin comprises a heterogeneous mixture of recombinant human gelatin polypeptides.

14. (Amended) The composition of claim 20 [1], wherein the recombinant human gelatin is obtained [derived] from one type of collagen free of any other collagen.

15. (Reiterated) The composition of claim 14, wherein the one type of collagen is selected from the group consisting of type I, type II, type III, type IV, type V, type VI, type VII, type VIII, type IX, type X, type XI, type XII, type XIII, type XIV, type XV, type XVI, type XVII, type XVIII, type XIX, and type XX collagen.

16. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin has an endotoxin level below 1.000 EU/mg.

17. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin has an endotoxin level [endotoxin level] below 0.500 EU/mg.

18. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin has an endotoxin level [endotoxin level] below 0.050 EU/mg.

19. (Amended) [The] A composition [of claim 1,] comprising a recombinant gelatin, wherein the recombinant gelatin has an endotoxin level [endotoxin level] below 0.005 EU/mg.

20. (Amended) [The] A composition [of claim 1, wherein the recombinant gelatin is] comprising a recombinant human gelatin.

21. (Amended) A recombinant gelatin comprising the amino acid sequence [selected from the group consisting of SEQ ID NOs:15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 31, and 33] of SEQ ID NO:18.

30. (Amended) A recombinant gelatin comprising the amino acid sequence [selected from the group consisting of SEQ ID NOs:26, 27, 28, and 29] of SEQ ID NO:29.

42. (Amended) A binding agent comprising the recombinant human gelatin of claim 20.

43. (Amended) An encapsulant comprising the recombinant human gelatin of claim 20.

44. (Amended) A stabilizing agent comprising the recombinant human gelatin of claim 20.

45. (Amended) A film-forming agent comprising the recombinant human gelatin of claim 20.

46. (Amended) A moisturizing agent comprising the recombinant human gelatin of claim 20.

47. (Amended) An emulsifier comprising the recombinant human gelatin of claim 20.

48. (Amended) A thickening agent comprising the recombinant human gelatin of claim 20.

49. (Amended) A gelling agent comprising the recombinant human gelatin of claim 20.

50. (Amended) A colloidal agent comprising the recombinant human gelatin of claim 20.

51. (Amended) An adhesive agent comprising the recombinant human gelatin of claim 20.

53. (Amended) [The] A pharmaceutical composition [of claim 52, wherein the recombinant gelatin is human recombinant gelatin] comprising a recombinant human gelatin.

54. (Amended) A hard gel capsule comprising the recombinant human gelatin of claim 20.

55. (Amended) A soft gel capsule comprising the recombinant human gelatin of claim 20.

56. (Amended) A plasma expander comprising the recombinant human gelatin of claim 20.

57. (Amended) A colloidal volume replacement material comprising the recombinant human gelatin of claim 20.

58. (Amended) A graft coating comprising the recombinant human gelatin of claim 20.

59. (Amended) A medical sponge comprising the recombinant human gelatin of claim 20.

60. (Amended) A medical plug comprising the recombinant human gelatin of claim 20.

61. (Amended) A pharmaceutical stabilizer comprising the recombinant human gelatin of claim 20.

62. (Amended) A microcarrier [micro-carrier] comprising the recombinant human gelatin of claim 20.

64. (Amended) An edible composition comprising the recombinant human gelatin of claim 20.

65. (Amended) A protein supplement comprising the recombinant human gelatin of claim 20

66. (Amended) A fat substitute comprising the recombinant human gelatin of claim 20.

67. (Amended) A nutritional supplement comprising the recombinant human gelatin of claim 20.

68. (Amended) An edible coating comprising the recombinant human gelatin of claim 20.

69. (Amended) A photographic composition comprising the recombinant gelatin of claim 7 [partially-hydroxylated recombinant gelatin].

70. (Amended) A photographic composition comprising the recombinant human gelatin of claim 20 [fully-hydroxylated recombinant gelatin].

71. (Amended) A cosmetic composition comprising the recombinant human gelatin of claim 20.

72. (Amended) An industrial composition comprising the recombinant human gelatin of claim 20.

73. (Amended) A cell culture composition comprising the recombinant human gelatin of claim 20.

74. (Amended) A composition for laboratory use comprising the recombinant human gelatin of claim 20.

75. (New) The pharmaceutical stabilizer of claim 61, wherein the pharmaceutical stabilizer is a vaccine stabilizer.